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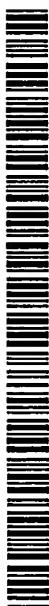
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

**WO 01/018250 A3**

(54) Title: SINGLE NUCLEOTIDE POLYMORPHISMS IN GENES

(57) Abstract: The invention provides nucleic acid segments of the human genome, particularly nucleic acid segments from a gene, including polymorphic sites. Allele-specific primers and probes hybridizing to regions flanking or containing these sites are also provided. The nucleic acids, primers and probes are used in applications such as phenotype correlations, forensics, paternity testing, medicine and genetic analysis. A role for the thrombospondin gene(s) in vascular disease is also disclosed. Use of single nucleotide polymorphisms in the thrombospondin gene(s) for diagnosis, prediction of clinical course and treatment response, development of therapeutics and development of cell-culture-based and animal models for research and treatment are disclosed.

**INTERNATIONAL SEARCH REPORT**

Inte... Application No  
PCT/US 00/24503

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C12Q1/68 C07K14/47 C07K14/78		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) <b>IPC 7 C07K C12Q</b>		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) <b>MEDLINE, SEQUENCE SEARCH, BIOSIS, EPO-Internal</b>		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 750 502 A (KLAR AVIHU ET AL) 12 May 1998 (1998-05-12) SEQ ID NO:20 ---	1-30
A	POLYMEROPoulos M H ET AL: "DINUCLEOTIDE REPEAT POLYMORPHISM AT THE HUMAN THROMBOSpondin GENE THBS1" NUCLEIC ACIDS RESEARCH, vol. 18, no. 24, 1990, page 7467 XP002188932 ISSN: 0305-1048 abstract ---	1-30 -/-
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		<input checked="" type="checkbox"/> Patent family members are listed in annex.
<b>* Special categories of cited documents :</b> "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed		
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search <b>5 February 2002</b>		Date of mailing of the international search report <b>15. 05. 2002</b>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel: (+31-70) 340-2040, Tx: 31 651 epo nl. Fax: (+31-70) 340-3016		Authorized officer <b>van Klompenburg, W</b>

## INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/US 00/24503

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WANG D G ET AL: "Large-scale identification, mapping, and genotyping of single-nucleotide polymorphisms in the human genome"  SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 280, 1998, pages 1077-1082,  XP002089398  ISSN: 0036-8075  the whole document</p> <p>---</p>	1-30
A	<p>FAN J ET AL: "Genetic mapping: Finding and analyzing single-nucleotide polymorphisms with high-density DNA arrays"  AMERICAN JOURNAL OF HUMAN GENETICS, UNIVERSITY OF CHICAGO PRESS, CHICAGO,, US, vol. 61, no. 4, SUPPL, 1 October 1997 (1997-10-01), page 1601  XP002089397  ISSN: 0002-9297  abstract</p> <p>-----</p>	1-30

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/24503

### Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-30

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1, claims 1-30

A method for predicting or diagnosing a vascular disease comprising; determining the nucleotide present at position 2210 of the thrombospondin 1 gene (SEQ ID NO:1). A nucleic acid molecule, a peptide (SEQ ID NO:2). A method for predicting or diagnosing a vascular disease comprising; determining the amino acid at position 700 of thrombospondin-1.

Invention 2, claims 31-60

A method for predicting or diagnosing a vascular disease comprising; determining the nucleotide present at position 2210 of the thrombospondin-4 gene (SEQ ID NO:3). A nucleic acid molecule, a peptide (SEQ ID NO:4). A method for predicting or diagnosing a vascular disease comprising; determining the amino acid at position 700 of thrombospondin-4.

Inventions 3 - 2547, claims 61-72

A nucleic acid molecule, an isolated gene product. A method of analyzing a nucleic acid sample. Every invention is characterised by each individual sequence of table 1 (corresponding to SEQ ID NO: 7-2551).

## INTERNATIONAL SEARCH REPORT

Inte	I Application No
PCT/US 00/24503	

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
US 5750502	A 12-05-1998	US	5279966 A	18-01-1994
		AU	713198 B2	25-11-1999
		AU	1269897 A	15-05-1997
		AU	677185 B2	17-04-1997
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		WO	9320196 A1	14-10-1993
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